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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/905,083	07/13/2001	Timothy I. O'Brien	D6223CIP/C/D	4623

7590 04/04/2006  
Dr. Benjamin Adler  
Adler & Associates  
8011 Candle Lane  
Houston, TX 77071

EXAMINER

BLANCHARD, DAVID J

ART UNIT PAPER NUMBER

1643

DATE MAILED: 04/04/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application No.

09/905,083

Applicant(s)

O'BRIEN, TIMOTHY I.

Examiner

David J. Blanchard

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 23 January 2006.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 26, 30 and 31 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 26, 30 and 31 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)  | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                                   | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

### **DETAILED ACTION**

1. Claims 1-25, 27-29 and 32-39 are cancelled.  
Claim 31 has been amended.
2. Claims 26 and 30-31 are pending and under examination.
3. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

### ***Response to Arguments***

4. The rejection of claims 30-31 under 35 U.S.C. 112, first paragraph, because the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with the claims is maintained.

The response filed 1/23/2006 states that claim 31 has been amended to delete the term "suspected or at risk of getting cancer" to overcome the rejection. This has been fully considered but is not found persuasive. Although the amendment to claim 31 has deleted the term "suspected or at risk of getting cancer", the claim has also been amended to add "at risk for ovarian cancer or prostate cancer", which is merely another way of stating the deleted claim term and as such the rejection is maintained for reasons of record. It is not clear what was intended by the amendment to claim 31, however, amending the claim to delete the phrase "at risk for ovarian cancer or prostate cancer" would overcome this rejection.

5. The rejection of claims 26 and 30-31 under 35 U.S.C. 112, first paragraph, because the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with the claims is maintained.

The response filed 1/23/2006 has been carefully considered, but is deemed not to be persuasive. The response states that methods for identifying peptides useful for the immune stimulation are well known and generally available to one of ordinary skill in the art and HLA class I binding motifs can be identified using computer programs, which applicant has used to identify that the peptides of SEQ ID Nos:31, 32, 33, 34, 35, 36, 80, 86 and 99 contain motifs for HLA class I molecules. Applicant previously submitted a Declaration under 37 CFR 1.132 by Dr. Timothy J. O'Brien (filed 2/19/2003) which established that SCCE peptide 5-13 (SEQ ID NO:33) and SCCE peptide 123-131 (SEQ ID NO:32) induce CD8+ CTL responses in vitro. Applicant asserts that the claims are not broad and testing the claimed SCCE peptides using the disclosed method for their effectiveness at inducing CTL responses would not require undue experimentation. In response to the cited art of Hansson et al, Applicant submits a second declaration under 37 CFR 1.132, which provides evidence that the SCCE peptide 5-13 (SEQ ID NO:33) of the signal peptide of SCCE effectively generates CTLs that lyse ovarian cancer cells when the cells were not pulsed initially with the SCCE peptide of SEQ ID NO:33 providing evidence that the SCCE 5-13 peptide of the signal peptide is naturally expressed, processed and presented by ovarian tumor cells. The Declarations under 37 CFR 1.132 filed 2/19/2003 and 1/23/2006 are insufficient to overcome the rejection

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of claims 26, 30 and 31 based upon insufficiency of the disclosure under 35 U.S.C. 112, first paragraph as set forth in the last Office action because the showing is not commensurate in scope with the claims. For example, the Declarations submit evidence that SCCE peptide 5-13 (SEQ ID NO:33) and SCCE peptide 123-131 (SEQ ID NO:32) induce CD8+ CTL responses in vitro, however, the claims encompass SCCE peptides other than SEQ ID Nos:32 and 33 that do not contain amino acids 5-13 or 123-131 of SCCE. Further, the claims encompass SCCE dendritic cell immunotherapy in cancer patients (i.e., "reintroduced into said individual subsequent to exposure") while the showings in the Declarations are limited to in vitro evidence. Applicant also submits the art of Dhodapkar et al in support of the assertion that cell based therapy to treat malignant conditions were known at the time the instant invention was made and dendritic cell therapy or the reintroduction of activated dendritic cells is well established and does not require undue experimentation. The examiner acknowledges that a large body of art exists as it pertains to dendritic cell adaptive immunotherapy, however, the state of the art is such that all of the parameters for the clinical application of dendritic cells in the treatment of cancer have not been standardized and are not yet predictable. For, example the art of Cranmer et al (Cancer Immunology and Immunotherapy, 53(4):275-306, April 2004) teaches that most clinical trials to date have not yielded data from which firm conclusions can be drawn and optimal parameters in humans remain to be established (see abstract). At page 277, left column, Cranmer et al teach that many routes of vaccination have been utilized, but there is limited information regarding the optimal route, optimal dose has not been determined, maximal cell dose is limited, at

present, by the ability to culture the cells in large numbers, there is no standard or optimal schedule for dendritic cell administration, the use of maintenance vaccinations, and the use of revaccination after failure have not been addressed (see also pg. 303, left column). Further, Soruri et al (The International Journal of Biochemistry and Cell Biology, 37(2):241-245, February 2005) teach that despite the wide use monocyte-derived dendritic cells (MoDC) for experimental and clinical immunotherapy, unequivocal proof for clinical efficiency of MoDC-based anti-tumor vaccinations is still missing and MoDC may not represent the equivalent of migratory dendritic cells in vivo limiting their use as magic bullets in tumor immunotherapy (see abstract). More importantly, Applicant has not provided any guidance or direction regarding any of the above parameters for reintroducing SCCE activated dendritic cells in cancer patients and the instant specification does not provide any in vitro data regarding the efficacy of computer predicted motifs for HLA class I molecules to induce SCCE-specific CTL. The selection of the SCCE peptides of SEQ ID Nos:31-36, 80, 86 and 99 using a computer program and the showing that SEQ ID Nos:32 and 33 are effective at inducing specific CD8+ CTL responses in vitro is insufficient to support the enablement of the full scope of the claims because the specification does not provide guidance as it pertains to different dendritic cell sources, different precursor cell mobilization methods, different dendritic cell culture methods and different cytokine mixtures to induce their development, different durations, concentrations and other parameters in the antigen exposure process, different routes, schedules and cell doses for immunization, non-standardized means of assessing induced immune responses and incomplete

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description of clinical responses. Applicant essentially leaves this significant portion of their invention to those skilled in the art to begin to discover for themselves how to effectively practice the claimed method, which is not predictable or standardized in the current state of the art and such experimentation is labor- and resource-intensive according to Cranmer et al (see abstract). The evidence of record does not show that a skilled artisan would have been able to carry out the steps required to practice the full scope of claims, which encompasses reintroducing activated dendritic cells into an individual/patient for producing activated T cells in vivo toward SCCE that effectively treats any disorder, in particular, ovarian and prostate cancer, without undue experimentation.

Applicant also argues the cited art of Riott et al, Geysen and Wang (all of record) stating that Geysen used all possible 9-mers and 12-mers of the MPB70 sequence to test for T-cell proliferation and the peptides of Wang were prepared based solely on the binding motif of HLA-A31 and not on the basis of a computer program that takes into account affinity binding kinetics such as the program used in the instant application. Applicant concludes it would be inappropriate to assume that the method used by the applicant will not correctly recognize molecules that can bind HLA class I molecules, especially in view of the fact that two such peptides (SEQ ID Nos:32 and 33) were shown to bind HLA class I molecules and activate SCCE-specific T cells. This has been fully considered but is not found persuasive. As set forth in the previous Office Action, the art of Wang et al (US Patent 5,840,839, of record) is evidence that finding a peptide that binds to an MHC molecule and stimulates an immune response is not a trivial

matter. The '839 patent at columns 19-20 and table 1 teach that the various candidate T cell epitopes selected based on theoretical binding motifs of one class of MHC molecule, i.e., HLA-A31 do not work when they are experimentally tested as shown in Table 1. Further, the art of Geysen (US Patent 5,539,084, of record) demonstrates that even for peptides of similar size derived from the same "parent" polypeptide, not all will be capable of interacting with T-cells (column 2, lines 5-9 and Figure 6), thus demonstrating the degree of uncertainty in the art for predicting which subsets or portions of a larger polypeptide will be capable of interacting with or stimulating T-cells. While Applicant is not claiming broadly, Applicant has not provided any objective evidence demonstrating that the claimed method of producing activated T cells against the theoretical SCCE peptides of SEQ ID Nos:31, 34, 35, 36, 80, 86 and 99 effectively stimulate T cells that induce peptide-specific cytotoxicity in ovarian and prostate cancer patients.

In view of the lack of predictability of the art to which the invention pertains, the lack of established clinical protocols for effective dendritic cell therapies, undue experimentation would be required to practice the claimed methods with a reasonable expectation of success, absent a specific and detailed description in applicant's specification of how to effectively practice the claimed methods and absent working examples providing evidence which is reasonably predictive that the claimed methods of dendritic cell immunotherapy to treat ovarian and prostate cancer patients in particular, commensurate in scope with the claimed invention.



***Conclusions***

6. No claim is allowed.
7. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to David J. Blanchard whose telephone number is (571) 272-0827. The examiner can normally be reached at Monday through Friday from 8:00 AM to 6:00 PM, with alternate Fridays off. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew, can be reached at (571) 272-0787. The official fax number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR.

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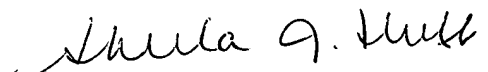
Status information for unpublished applications is available through Private PAIR only.

For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should

you have questions on access to the Private PAIR system, contact the Electronic

Business Center (EBC) at 866-217-9197 (toll-free).

Respectfully,  
David J. Blanchard  
571-272-0827



SHEELA HUFF  
PRIMARY EXAMINER